Mouse SCNT ESCs Have Lower Somatic Mutation Load Than Syngeneic iPSCs.

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Public Summary:
This publication reports the first direct comparison of the genomic stability of two nuclear reprogramming methods to generate pluripotent stem cells. The data indicate that the more physiologically relevant method give rise to pluripotent stem cells harboring fewer gene mutations.

Scientific Abstract:
Ectopic expression of reprogramming factors has been widely adopted to reprogram somatic nucleus into a pluripotent state (induced pluripotent stem cells [iPSCs]). However, genetic aberrations such as somatic gene mutation in the resulting iPSCs have raised concerns regarding their clinical utility. To test whether the increased somatic mutations are primarily the by-products of current reprogramming methods, we reprogrammed embryonic fibroblasts of inbred C57BL/6 mice into either iPSCs (8 lines, 4 previously published) or embryonic stem cells (ESCs) with somatic cell nuclear transfer (SCNT ESCs; 11 lines). Exome sequencing of these lines indicates a significantly lower mutation load in SCNT ESCs than iPSCs of syngeneic background. In addition, one SCNT-ESC line has no detectable exome mutation, and two pairs of SCNT-ESC lines only have shared preexisting mutations. In contrast, every iPSC line carries unique mutations. Our study highlights the need for improving reprogramming methods in more physiologically relevant conditions.